

## INVENTOR SEARCH

=&gt; d 15 ibib abs 1-3

L5 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2010 ACS on STN  
 ACCESSION NUMBER: 2008:317174 HCAPLUS Full-text  
 DOCUMENT NUMBER: 149:432441  
 TITLE: Tissue Engineering by Self-Assembly of Cells Printed  
 into Topologically Defined Structures  
 AUTHOR(S): Jakab, Karoly; Norotte, Cyrille; Damon,  
 Brook; Marga, Francoise; Neagu, Adrian;  
 Besch-Williford, Cynthia L.; Kachurin, Anatoly;  
 Church, Kenneth H.; Park, Hyoungshin; Mironov,  
 Vladimir; Markwald, Roger; Vunjak-Novakovic,  
 Gordana; Forgacs, Gabor  
 CORPORATE SOURCE: Department of Physics, University of Missouri,  
 Columbia, MO, USA  
 SOURCE: Tissue Engineering, Part A (2008), 14(3), 413-421  
 CODEN: TEPAB9; ISSN: 1937-3341  
 PUBLISHER: Mary Ann Liebert, Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Understanding the principles of biol. self-assembly is indispensable for developing efficient strategies to build living tissues and organs. We exploit the self-organizing capacity of cells and tissues to construct functional living structures of prescribed shape. In our technol., multicellular spheroids (bio-ink particles) are placed into biocompatible environment (bio-paper) by the use of a three-dimensional delivery device (bio-printer). Our approach mimics early morphogenesis and is based on the realization that the genetic control of developmental patterning through self-assembly involves phys. mechanisms. Three-dimensional tissue structures are formed through the postprinting fusion of the bio-ink particles, in analogy with early structure-forming processes in the embryo that utilize the apparent liquid-like behavior of tissues composed of motile and adhesive cells. We modeled the process of self-assembly by fusion of bio-ink particles, and employed this novel technol. to print extended cellular structures of various shapes. Functionality was tested on cardiac constructs built from embryonic cardiac and endothelial cells. The postprinting self-assembly of bio-ink particles resulted in synchronously beating solid tissue blocks, showing signs of early vascularization, with the endothelial cells organized into vessel-like conduits.

OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS  
 RECORD (16 CITINGS)  
 REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2010 ACS on STN  
 ACCESSION NUMBER: 2004:599196 HCAPLUS Full-text  
 DOCUMENT NUMBER: 142:162358  
 TITLE: Organ printing: Fiction or science  
 AUTHOR(S): Jakab, Karoly; Neagu, Adrian;  
 Mironov, Vladimir; Forgacs, Gabor  
 CORPORATE SOURCE: Department of Physics, University of Missouri,  
 Columbia, MO, 65211, USA  
 SOURCE: Biorheology (2004), 41(3,4), 371-375  
 CODEN: BRHLAU; ISSN: 0006-355X  
 PUBLISHER: IOS Press  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Aggregates of living cells (i.e. model tissue fragments) under appropriate conditions fuse like liquid drops. According to Steinberg's differential adhesion

hypothesis (DAH), this may be understood by assuming that cells are motile and tissues made of such cells possess an effective surface tension. Here the authors show that based on these properties 3-dimensional cellular structures of prescribed shape can be constructed by a novel method: cell aggregate printing. Spherical aggregates of similar size made of cells with known adhesive properties were prepared. Aggregates were embedded into biocompatible gels. When the cellular and gel properties, as well as the symmetry of the initial configuration were appropriately adjusted the contiguous aggregates fused into ring-like organ structures. To elucidate the driving force and optimal conditions for this pattern formation, Monte Carlo simulations based on a DAH motivated model were performed. The simulations reproduced the exptl. observed cellular arrangements and revealed that the control parameter of pattern evolution is the gel-tissue interfacial tension, an exptl. accessible parameter.

OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)  
 REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:231218 HCAPLUS Full-text

DOCUMENT NUMBER: 140:231677

TITLE: Engineering biological structures of prescribed shape using self-assembling multicellular systems

AUTHOR(S): Jakab, Karoly; Neagu, Adrian; Mironov, Vladimir; Markwald, Roger R.; Forgacs, Gabor

CORPORATE SOURCE: Department of Physics, University of Missouri, Columbia, MO, 65211, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2004), 101(9), 2864-2869  
 CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Self-assembly is a fundamental process that drives structural organization in both inanimate and living systems. It is in the course of self-assembly of cells and tissues in early development that the organism and its parts eventually acquire their final shape. Even though developmental patterning through self-assembly is under strict genetic control, it is clear that ultimately it is phys. mechanisms that bring about the complex structures. Here, we show, both exptl. and by using computer simulations, how tissue liquidity can be used to build tissue constructs of prescribed geometry in vitro. Spherical aggregates containing many thousands of cells, which form because of tissue liquidity, were implanted contiguously into biocompatible hydrogels in circular geometry. Depending on the properties of the gel, upon incubation, the aggregates either fused into a toroidal 3D structure or their constituent cells dispersed into the surrounding matrix. The model simulations, which reproduced the exptl. observed shapes, indicate that the control parameter of structure evolution is the aggregate-gel interfacial tension. The model-based anal. also revealed that the observed toroidal structure represents a metastable state of the cellular system, whose lifetime depends on the magnitude of cell-cell and cell-matrix interactions. Thus, these constructs can be made long-lived. We suggest that spherical aggregates composed of organ-specific cells may be used as "bio-ink" in the evolving technol. of organ printing. OS.CITING REF

COUNT: 60 THERE ARE 60 CAPLUS RECORDS THAT CITE THIS RECORD (60 CITINGS)  
 REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

## RESULTS FROM SEARCHES IN CAPLUS, MEDLINE, BIOSIS, EMBASE, AND DRUGU

=&gt; d que stat 121

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L7      745393 SEA FILE=HCAPLUS ABB=ON  ?BIOCOMPATIBL? OR ?MATRIX? OR
        ?MATRICES?
L8      588 SEA FILE=HCAPLUS ABB=ON  L7 AND CELL(W)AGGREGAT?
L9      172 SEA FILE=HCAPLUS ABB=ON  L8 AND (?SCAFFOLD? OR ?LAYER? OR
        ?THREE?(W)?DIMENSIONAL?)
L11     87 SEA FILE=HCAPLUS ABB=ON  L9 AND (NON(W)?RANDOM? OR ?CYLIND? OR
        ?SPHER? OR (?SINGL? OR ?MULT?)(3A)CELL? OR FIBROBLAST? OR
        ?MESENCHYMA?)
L14     87 SEA FILE=HCAPLUS ABB=ON  L11 AND (NON(W)?RANDOM? OR ?CYLIND?
        OR ?SPHER? OR (?SINGL? OR ?MULT?)(3A)CELL? OR FIBROBLAST? OR
        ?MESENCHYMA?)
L15     35 SEA FILE=HCAPLUS ABB=ON  L14 AND (PRD<20040224 OR PD<20040224)

L16     168 SEA L15
L17     19 SEA FILE=HCAPLUS ABB=ON  L11 AND (GEL? OR ?PHOTOSENSITIV? OR
        ?THERMO?(W)?REVERSIBL? OR PH(W)?SENSITIV?)
L18     87 SEA FILE=HCAPLUS ABB=ON  L14 OR L17
L19     35 SEA FILE=HCAPLUS ABB=ON  L18 AND (PRD<20040224 OR PD<20040224)

L20     9 SEA L16 AND ?TISSUE?(W) ?ENGINEER?
L21     41 DUP REMOV L19 L20 (3 DUPLICATES REMOVED)

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=&gt; d ibib abs 121 1-41

L21 ANSWER 1 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:235284 HCAPLUS Full-text

DOCUMENT NUMBER: 140:301042

TITLE: Fibronectin ~~matrix~~ assembly regulates $\alpha 5\beta 1$ -mediated cell cohesion

AUTHOR(S): Robinson, Elizabeth E.; Foty, Ramsey A.; Corbett, Siobhan A.

CORPORATE SOURCE: Department of Surgery, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ, 08903, USA

SOURCE: Molecular Biology of the Cell (2004), 15(3), 973-981

CODEN: MBCEEV; ISSN: 1059-1524

PUBLISHER: American Society for Cell Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Integrin-extracellular ~~matrix~~ (ECM) interactions in two-dimensional (2D) culture systems are widely studied. Less understood is the role of the ECM in promoting intercellular cohesion in ~~three-dimensional~~ (3D) environments. We have demonstrated that the  $\alpha 5\beta 1$ -integrin mediates strong intercellular cohesion of 3D cellular aggregates. To further investigate the mechanism of  $\alpha 5\beta 1$ -mediated cohesivity, we used a series of chimeric  $\alpha 5\beta 1$ -integrin-expressing ~~cells~~ cultured as ~~multilayer cellular~~ aggregates. In these cell lines, the  $\alpha 5$  subunit cytoplasmic domain distal to the GFFKR sequence was truncated, replaced with that of the integrin  $\alpha 4$ , the integrin  $\alpha 2$ , or maintained intact. Using these cells,  $\alpha 5\beta 1$ -integrin-mediated ~~cell aggregation~~, compaction and cohesion were determined and correlated with FN ~~matrix~~ assembly. The data presented demonstrate that cells cultured in the absence of external mech. support can assemble a FN ~~matrix~~ that promotes integrin-mediated aggregate compaction and cohesion. Further, inhibition of FN ~~matrix~~ assembly blocks the intercellular assocns. required for compaction,

resulting in cell dispersal. These results demonstrate that FN ~~matrix~~ assembly contributes significantly to tissue cohesion and represents an alternative mechanism for regulating tissue architecture. OS.CITING REF COUNT: 29 THERE ARE 29 CAPLUS RECORDS THAT CITE THIS

RECORD (29 CITINGS)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:614467 HCAPLUS Full-text

DOCUMENT NUMBER: 141:415941

TITLE: A ~~three-dimensional~~ nanofibrous scaffold for cartilage tissue engineering using human ~~mesenchymal~~ stem cells

AUTHOR(S): Li, Wan-Ju; Tuli, Richard; Okafor, Chukwuka; Derfoul, Assia; Danielson, Keith G.; Hall, David J.; Tuan, Rocky S.

CORPORATE SOURCE: Department of Health and Human Services, Cartilage Biology and Orthopaedics Branch, National Institute of Arthritis, and Musculoskeletal and Skin Diseases, National Institute of Health, Bethesda, MD, 20892, USA

SOURCE: Biomaterials (2004), Volume Date 2005, 26(6), 599-609

CODEN: BIMADU; ISSN: 0142-9612

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The utilization of adult stem cells in tissue engineering is a promising solution to the problem of tissue or organ shortage. Adult bone marrow derived ~~mesenchymal~~ stem cells (MSCs) are undifferentiated, ~~multipotential~~ cells which are capable of giving rise to chondrocytes when maintained in a ~~three-dimensional~~ culture and treated with members of the transforming growth factor- $\beta$  (TGF- $\beta$ ) family of growth factors. In this study, we fabricated a nanofibrous scaffold (NFS) made of a synthetic biodegradable polymer, poly(~~vepsiln~~-caprolactone) (PCL), and examined its ability to support in vitro chondrogenesis of MSCs. The electrospun PCL porous scaffold was constructed of uniform, randomly oriented nanofibers with a diameter of 700 nm, and structural integrity of this scaffold was maintained over a 21-day culture period. MSCs cultured in NFSs in the presence of TGF- $\beta$ 1 differentiated to a chondrocytic phenotype, as evidenced by chondrocyte-specific gene expression and synthesis of cartilage-associated extracellular ~~matrix~~ (ECM) proteins. The level of chondrogenesis observed in MSCs seeded within NFSs was comparable to that observed for MSCs maintained as cell aggregates or pellets, a widely used culture protocol for studying chondrogenesis of MSCs in vitro. Due to the phys. nature and improved mech. properties of NFSs, particularly in comparison to cell pellets, the findings reported here suggest that the PCL NFS is a practical carrier for MSC transplantation, and represents a candidate scaffold for cell-based tissue engineering approaches to cartilage repair. OS.CITING REF COUNT: 261 THERE ARE 261 CAPLUS RECORDS THAT CITE THIS

RECORD (263 CITINGS)

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 3 OF 41 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2004395674 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 15299269

TITLE: Organ printing: fiction or science.

AUTHOR: Jakab Karoly; Neagu Adrian; Mironov Vladimir; Forgacs Gabor

CORPORATE SOURCE: Department of Physics, University of Missouri, Columbia, MO 65211, USA.

SOURCE: Biorheology, (2004) Vol. 41, No. 3-4, pp. 371-5.

Journal code: 0372526. ISSN: 0006-355X. L-ISSN: 0006-355X.  
 PUB. COUNTRY: Netherlands  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200412  
 ENTRY DATE: Entered STN: 10 Aug 2004  
 Last Updated on STN: 20 Dec 2004  
 Entered Medline: 14 Dec 2004

AB Aggregates of living cells (i.e. model tissue fragments) under appropriate conditions fuse like liquid drops. According to Steinberg's differential adhesion hypothesis (DAH), this may be understood by assuming that cells are motile and tissues made of such cells possess an effective surface tension. Here we show that based on these properties three-dimensional cellular structures of prescribed shape can be constructed by a novel method: cell aggregate printing. Spherical aggregates of similar size made of cells with known adhesive properties were prepared. Aggregates were embedded into biocompatible gels. When the cellular and gel properties, as well as the symmetry of the initial configuration were appropriately adjusted the contiguous aggregates fused into ring-like organ structures. To elucidate the driving force and optimal conditions for this pattern formation, Monte Carlo simulations based on a DAH motivated model were performed. The simulations reproduced the experimentally observed cellular arrangements and revealed that the control parameter of pattern evolution is the gel-tissue interfacial tension, an experimentally accessible parameter.

L21 ANSWER 4 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:258686 HCAPLUS Full-text

DOCUMENT NUMBER: 141:51673

TITLE: Ovarian carcinoma ascites spheroids adhere to extracellular matrix components and mesothelial cell monolayers

AUTHOR(S): Burleson, Kathryn M.; Casey, Rachael C.; Skubitz, Keith M.; Pambuccian, Stephan E.; Oegema, Theodore R.; Skubitz, Amy P. N.

CORPORATE SOURCE: Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, MN, 55455, USA

SOURCE: Gynecologic Oncology (2004), 93(1), 170-181  
 CODEN: GYNOA3; ISSN: 0090-8258

PUBLISHER: Elsevier Science

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Ovarian carcinoma cells form multicellular aggregates, or spheroids, in the peritoneal cavity of patients with advanced disease. The current paradigm that ascites spheroids are non-adhesive leaves their contribution to ovarian carcinoma dissemination undefined. Here, spheroids obtained from ovarian carcinoma patients' ascites were characterized for their ability to adhere to mols. encountered in the peritoneal cavity, with the goal of establishing their potential to contribute to ovarian cancer spread. Spheroids were recovered from the ascites fluid of 11 patients with stage III or stage IV ovarian carcinoma. Adhesion assays to extracellular matrix (ECM) proteins and human mesothelial cell monolayers were performed for each of the ascites spheroid samples. Subsequently, inhibition assays were performed to identify the cell receptors involved. Most ascites samples adhered moderately to fibronectin and type I collagen, with reduced adhesion to type IV collagen and laminin. Monoclonal antibodies against the  $\beta$ 1 integrin subunit partially inhibited this adhesion. Ascites spheroids also adhered to hyaluronan. Addnl., spheroids adhered to live, but not fixed, human mesothelial cell monolayers, and this adhesion was partially mediated by  $\beta$ 1 integrins. The

cellular content of the ascites fluid has often been considered non-adhesive, but our findings are the first to suggest that patient-derived ascites ~~spheroids~~ can adhere to mesothelial extracellular ~~matrix~~ via  $\beta 1$  integrins, indicating that ~~spheroids~~ should not be ignored in the dissemination of ovarian cancer. OS.CITING

REF COUNT: 38 THERE ARE 38 CAPLUS RECORDS THAT CITE THIS  
RECORD (38 CITINGS)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 5 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:573745 HCAPLUS Full-text

DOCUMENT NUMBER: 140:187272

TITLE: Gland cell cultures into 3D hyaluronan-based  
~~scaffolds~~

AUTHOR(S): Zavan, B.; Cortivo, R.; Tonello, C.; Abatangelo, G.

CORPORATE SOURCE: Microbiology and Medical Biotechnology, Department of  
Histology, University of Padova, Italy

SOURCE: Journal of Materials Science: Materials in Medicine (   
2003), 14(8), 727-729

CODEN: JSMMEL; ISSN: 0957-4530

PUBLISHER: Kluwer Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In this study the authors report a preliminary investigation of the feasibility of non-woven/sponge fabrics of a hyaluronan derived biomaterials, benzyl ester of HA (HYAFF-11 FAB, Abano Terme, Italy) for the in vitro culture of rat hepatocytes and rat beta cells. Cell growth on hyaluronan derived biomaterials were tested in the presence of complete medium and in the presence of ECM (extracellular ~~matrix~~) secreted by ~~fibroblasts~~ previously cultured into the ~~scaffold~~. Hepatocytes and beta cells were extracted from rat liver/pancreas and seeded either on the HYAFF-11 ~~scaffold~~ alone, or on HYAFF-11 ~~scaffold~~ containing ECM. Direct assay of cell proliferation was performed with MTT test. For morphol. observations samples were stained with hematoxylin and eosin. The results obtained by MTT test showed that hepatocytes cultivated in both the above described conditions were able to proliferate up to 14 days and Langerhans islet up to 21 days. After this time, cells started to undergo apoptosis. The morphol. analyses showed ~~cell aggregation~~ in 3-dimensional structures promoted by the fibers of the biomaterial. The authors' results confirmed that HYAFF-11 meshes represent a suitable ~~scaffold~~ for hepatocyte adhesion/Langerhans islet organization and proliferation. In particular, the presence of a ~~fibroblast~~ secreted extracellular ~~matrix~~ improves the biol. property of the ~~scaffold~~.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD  
(4 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 6 OF 41 EMBASE COPYRIGHT (c) 2010 Elsevier B.V. All rights  
reserved on STN

ACCESSION NUMBER: 2003219391 EMBASE Full-text

TITLE: Collagen expression in ~~tissue engineered~~  
cartilage of aged human articular chondrocytes in a  
rotating bioreactor.

AUTHOR: Marlovits, Stefan, Dr. (correspondence); Tichy, B.;  
Schlegel, W.

CORPORATE SOURCE: Department of Traumatology, University of Vienna, Medical  
School, Waehringer Guertel 18-20, A-1090 Vienna, Austria.  
stefan.marlovits@akh-wien.ac.at

AUTHOR: Marlovits, Stefan, Dr. (correspondence); Truppe, M.

CORPORATE SOURCE: Ludwig Boltzmann Inst. Biomech./Cell, Vienna, Austria.  
stefan.marlovits@akh-wien.ac.at

AUTHOR: Gruber, D.  
 CORPORATE SOURCE: Institute of Zoology, Dept. of Ultrastructural Research,  
 University of Vienna, Vienna, Austria.  
 SOURCE: International Journal of Artificial Organs, (1 Apr  
 2003) Vol. 26, No. 4, pp. 319-330.  
 Refs: 35  
 ISSN: 0391-3988 CODEN: IJAODS  
 COUNTRY: Italy  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 027 Biophysics, Bioengineering and Medical  
 Instrumentation  
 029 Clinical and Experimental Biochemistry  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 12 Jun 2003  
 Last Updated on STN: 12 Jun 2003

AB This study describes the culture and ~~three-dimensional~~ assembly of aged human articular chondrocytes under controlled oxygenation and low shear stress in a rotating-wall vessel. Chondrocytes cultured in ~~monolayer~~ were released and placed without any ~~scaffold~~ as a ~~single cell~~ suspension in a rotating bioreactor for 12 weeks. Samples were analyzed with immunohistochemistry, molecular biology and electron microscopy. During serial ~~monolayer~~ cultures chondrocytes dedifferentiated to a "fibroblast-like" structure and produced predominantly collagen type I. When these dedifferentiated cells were transferred to the rotating bioreactor, the cells showed a spontaneous aggregation and formation of solid tissue during the culture time. Expression of collagen type II and other components critical for the extracellular cartilage ~~matrix~~ could be detected. Transmission electron microscopy revealed a fine network of randomly distributed collagen fibrils. This rotating bioreactor proves to be a useful tool for providing an environment that enables dedifferentiated chondrocytes to redifferentiate and produce a cartilage-specific extracellular ~~matrix~~.

L21 ANSWER 7 OF 41 MEDLINE on STN  
 ACCESSION NUMBER: 2003056779 MEDLINE Full-text  
 DOCUMENT NUMBER: PubMed ID: 12566253  
 TITLE: A ~~three-dimensional~~ cell culture model  
 for bovine endometrium: regeneration of a multicellular  
~~spheroid~~ using ascorbate.  
 AUTHOR: Yamauchi N; Yamada O; Takahashi T; Imai K; Sato T; Ito A;  
 Hashizume K  
 CORPORATE SOURCE: Laboratory of Reproductive Biology and Technology,  
 Department of Developmental Biology, National Institute of  
 Agrobiological Sciences, Ikenodai 2, Kukizaki,  
 Inashiki-gun, Ibaraki 305-8602, Japan.  
 SOURCE: Placenta, (2003 Feb-Mar) Vol. 24, No. 2-3, pp.  
 258-69.  
 Journal code: 8006349. ISSN: 0143-4004. L-ISSN: 0143-4004.  
 PUB. COUNTRY: England: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200307  
 ENTRY DATE: Entered STN: 5 Feb 2003  
 Last Updated on STN: 29 Jul 2003  
 Entered Medline: 28 Jul 2003

AB The development of a multicellular ~~spheroid~~ comprising bovine endometrial epithelial cells (BEE) and bovine endometrial stromal cells (BES) is described

in this study. The BES were cultured to confluence in medium with L -ascorbic acid phosphate magnesium salt n -hydrate (AsA-P) which stimulates collagen synthesis in BES. The BEE were co-cultured on a BES cell-sheet for 24h before detachment of the cell-sheet to generate a hetero-spheroid. After EDTA treatment and agitating with pipette, the floating cell-sheet shrank and became an aggregated cell mass in a few days; it finally formed a round-shaped hetero-spheroid composed of BES and BEE. Histological examination found that hetero-spheroids were covered with BEE on the outer layer. When cell viability was examined with TUNEL (terminal deoxynucleotidyl transferase mediated dUTP-biotin nick end labeling), no positive signal was detected in the spheroid for up to 10 days. Immunofluorescence observations showed that spheroids contained abundant extracellular matrices, including type-I, -III, -IV collagen, fibronectin, and laminin. PGF(2alpha) produced by hetero-spheroids in response to oxytocin was significantly higher than those produced by monolayer cultured BEE ( $P < 0.05$ ). MMPs were not detected in media from spheroids cultured for 5 days after detachment of the cell sheet. These results indicate that bovine endometrial cells have the capacity to regenerate as a multicellular spheroid after treatment with ascorbate in vitro. The spheroid displays an endometrium-mimic feature. Thus, we conclude that spheroids formed by BES and BEE are a useful in vitro model of bovine endometrium.

L21 ANSWER 8 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2003:472177 HCAPLUS Full-text

DOCUMENT NUMBER: 140:55901

TITLE: Method for generation of homogeneous multicellular tumor spheroids applicable to a wide variety of cell types

AUTHOR(S): Kelm, Jens M.; Timmins, Nicholas E.; Brown, Catherine J.; Fussenegger, Martin; Nielsen, Lars K.

CORPORATE SOURCE: Laboratory for Biological Engineering, Department of Chemical Engineering, University of Queensland, Brisbane, 4072, Australia

SOURCE: Biotechnology and Bioengineering (2003), 83(2), 173-180

CODEN: BIBIAU; ISSN: 0006-3592

PUBLISHER: John Wiley & Sons, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Multicellular tumor spheroids (MCTS) are used as organotypic models of normal and solid tumor tissue. Traditional techniques for generating MCTS, such as growth on nonadherent surfaces, in suspension, or on scaffolds, have a number of drawbacks, including the need for manual selection to achieve a homogeneous population and the use of nonphysiol. matrix compds. In this study the authors describe a mild method for the generation of MCTS, in which individual spheroids form in hanging drops suspended from a microtiter plate. The method was successfully applied to a broad range of cell lines and shows nearly 100% efficiency (i.e., one spheroid per drop). Using the hepatoma cell line, HepG2, the hanging drop method generated well-rounded MCTS with a narrow size distribution (coefficient of variation [CV] 10% to 15%, compared with 40% to 60% for growth on nonadherent surfaces). Structural anal. of HepG2 and a mammary gland adenocarcinoma cell line, MCF-7, composed spheroids, revealed highly organized, 3-dimensional, tissue-like structures with an extensive extracellular matrix. The hanging drop method represents an attractive for MCTS production, because it is mild, can be applied to a wide variety of cell lines, and can produce spheroids of a homogeneous size without the need for sieving or manual selection. The method has applications for basic studies of physiol. and metabolism, tumor biol., toxicol., cellular organization, and the development of bioartificial tissue.

OS.CITING REF COUNT: 91 THERE ARE 91 CAPLUS RECORDS THAT CITE THIS



RECORD (91 CITINGS)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 9 OF 41 MEDLINE on STN DUPLICATE 2  
 ACCESSION NUMBER: 2002466082 MEDLINE Full-text  
 DOCUMENT NUMBER: PubMed ID: 12226863  
 TITLE: Optimization of cardiac cell seeding and distribution in 3D  
 porous alginate ~~scaffolds~~.  
 AUTHOR: Dar Ayelet; Shachar Michal; Leor Jonathan; Cohen Smadar  
 CORPORATE SOURCE: Department of Biotechnology Engineering and The Institute  
 for Applied Biosciences, Ben-Gurion University of the  
 Negev, Beer-Sheva 84105 Israel.  
 SOURCE: Biotechnology and bioengineering, (2002 Nov 5)  
 Vol. 80, No. 3, pp. 305-12.  
 Journal code: 7502021. ISSN: 0006-3592. L-ISSN: 0006-3592.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200212  
 ENTRY DATE: Entered STN: 13 Sep 2002  
 Last Updated on STN: 17 Dec 2002  
 Entered Medline: 4 Dec 2002

AB Cardiac ~~tissue engineering~~ has evolved as a potential therapeutic approach to assist in cardiac regeneration. We have recently shown that ~~tissue-engineered~~ cardiac graft, constructed from cardiomyocytes seeded within an alginate ~~scaffold~~, is capable of preventing the deterioration in cardiac function after myocardial infarction in rats. The present article addresses cell seeding within porous alginate ~~scaffolds~~ in an attempt to achieve 3D high-density cardiac constructs with a uniform cell distribution. Due to the hydrophilic nature of the alginate ~~scaffold~~, its >90% porosity and interconnected pore structure, cell seeding onto the ~~scaffold~~ was efficient and short, up to 30 min. Application of a moderate centrifugal force during cell seeding resulted in a uniform cell distribution throughout the alginate ~~scaffolds~~, consequently enabling the loading of a large number of cells onto the 3D ~~scaffolds~~. The percent cell yield in the alginate ~~scaffolds~~ ranged between 60-90%, depending on cell density at seeding; it was 90% at seeding densities of up to  $1 \times 10^8$  cells/cm<sup>3</sup> ~~scaffold~~ and decreased to 60% at higher densities. The highly dense cardiac constructs maintained high metabolic activity in culture. Scanning electron microscopy revealed that the cells aggregated within the ~~scaffold~~ pores. Some of the aggregates were contracting spontaneously within the ~~matrix~~ pores. Throughout the culture there was no indication of cardiomyocyte proliferation within the ~~scaffolds~~, nor was it found in 3D cultures of cardiofibroblasts. This may enable the development of cardiac cocultures, without domination of cardiofibroblasts with time.

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L21 ANSWER 10 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN  
 ACCESSION NUMBER: 2001:906235 HCAPLUS Full-text  
 DOCUMENT NUMBER: 136:25166  
 TITLE: Method for composite cell-based implants using mineral  
 or polymeric microcarriers  
 INVENTOR(S): Frondoza, Carmelita G.; Hungerford, David S.; Shikani,  
 Alan H.; Domb, Abraham J.; Fink, David J.; Bloom,  
 Leonard  
 PATENT ASSIGNEE(S): Chondros, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 13 pp., Cont.-in-part of U. S. Ser. No. 825,632.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20010051834	A1	20011213	US 2001-922909	20010806 <--
US 20010014475	A1	20010816	US 2001-825632	20010404 <--
US 20020012705	A1	20020131	US 2001-929697	20010814 <--
US 6514522	B2	20030204		
US 20020123142	A1	20020905	US 2002-39718	20020103 <--
US 20020133235	A1	20020919	US 2002-66992	20020204 <--
US 20040117033	A1	20040617	US 2003-731366	20031209 <--
PRIORITY APPLN. INFO.:			US 1998-81016P	P 19980408 <--
			US 1998-104842P	P 19981020 <--
			US 1999-275319	A2 19990324 <--
			US 2000-712662	A2 20001114 <--
			US 2001-825632	A2 20010404 <--
			US 1999-165608P	P 19991115 <--
			US 2000-228855P	P 20000829 <--
			US 2001-922909	A3 20010806 <--

# ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB This invention is a method for the implantation of a combination of cells or cell-microcarrier aggregates wherein one component comprises a solid implantable construct and a second component comprises an injectable formulation. For example, in one embodiment, the solid implant may be first implanted to fill the majority of the cavity receiving the implant, and then cells or cell-microcarrier aggregates in an injectable format, with or without the addition of gelling materials to promote rapid gelling in situ, may be injected into spaces surrounding the solid implant in order to secure the solid implant in the site and/or to promote rapid adherence and/or integration of the solid implant to surrounding tissues. Also contemplated in this embodiment is that the cellular composition of the injectable component may differ from that of the solid component. For example, the solid implant may result from the culturing of chondrocytes on microcarriers or scaffolds, e.g., calcium carbonate, calcium phosphate or calcium sulfate, biopolymers, or synthetic polymers such as polylactic acid, polyglycolic or their copolymers, thereby resulting in an implant having cartilage-like properties, whereas the injectable cells or aggregates may result from the culturing of stem cells, resulting thereby in cells capable of producing cells of a chondrogenic, fibroblastic, myoblastic or osteoblastic phenotype. In this example, cells in the injectable aggregates may promote the fixation to or rapid integration of the solid cartilage implant into surrounding cartilage, connective tissue, muscle or bone, resp. A method of treating a skin lesion or nose or ear defects comprises filling the lesion or defect with a solid cell-containing implant along with an injectable cell-containing formulation. OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD

(10 CITINGS)

L21 ANSWER 11 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2001:815283 HCAPLUS Full-text

DOCUMENT NUMBER: 136:83764

TITLE: MMP inhibitors augment fibroblast adhesion through stabilization of focal adhesion contacts and up-regulation of cadherin function

AUTHOR(S): Ho, Andrew T.; Voura, Evelyn B.; Soloway, Paul D.; Watson, Katrina L. M.; Khokha, Rama

CORPORATE SOURCE: Department of Medical Biophysics and Department of Laboratory Medicine and Pathobiology, Ontario Cancer Institute, University of Toronto, University Health Network, Toronto, ON, M5G 2M9, Can.

SOURCE: Journal of Biological Chemistry (2001), 276(43), 40215-40224  
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Increased pericellular proteolysis due to an imbalance between MMPs (matrix metalloproteinases) and TIMPs (tissue inhibitors of metalloproteinases) promotes early stages of tumorigenesis. We have reported that TIMP-1 down-regulation confers tumorigenicity on immortal Swiss 3T3 fibroblasts. In pursuit of the mechanism involved in this transformation, we asked whether MMP inhibitors modulate contact inhibition and cell adhesion, because the dysregulation of these events is essential for cellular transformation. Using both genetic and biochem. means, we demonstrate that MMP inhibitors regulate fibroblast cell adhesion. TIMP-1 down-regulated cells formed dense, multilayered colonies, suggesting a loss of contact inhibition. Recombinant TIMP-1 and synthetic MMP inhibitors (MMPi) restored normal cell contact and d. of these cells in a dose-dependent manner. Consequently, the effect of MMPi on both cell-extracellular matrix (ECM) and cell-cell adhesion were investigated. Upon MMPi treatment, p125FAK was redistributed, together with vinculin, to points of cell-ECM contact. Furthermore, phosphorylation of p125FAK was restored to levels similar to that of wild type. In parallel, MMPi treatment increased cadherin levels and stabilized cadherin-mediated cell-cell contacts. Moreover, enhanced cadherin function was evident as increased calcium-dependent cell-cell aggregation and co-localization of cadherin and  $\beta$ -catenin at the cell membrane. We also obtained independent evidence of altered cadherin function using timp-1/- mouse embryonic fibroblasts. Our data provide provocative evidence that increased pericellular proteolysis impacts cell adhesion systems to offset normal contact inhibition, with subsequent effects on cell transformation and tumorigenesis. OS.CITING REF COUNT: 45 THERE ARE 45 CAPLUS RECORDS THAT CITE THIS

REFERENCE COUNT: 69 RECORD (45 CITINGS)  
THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 12 OF 41 BIOSIS COPYRIGHT (c) 2010 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:463421 BIOSIS Full-text

DOCUMENT NUMBER: PREV200100463421

TITLE: Regulation of cell proliferation using tissue engineering in MIN6 cells.

AUTHOR(S): Kinoshita, Naoko [Reprint author]; Echigo, Yoshiya; Shinohara, Sigeo; Gu, Yuanjun; Miyazaki, Junichi; Inoue, Kazutomo; Imamura, Masayuki

CORPORATE SOURCE: 53 Shogoin Kawaharacho Sakyo-ku, Kyoto, 606-8507, Japan  
naok@frontier.kyoto-u.ac.jp

SOURCE: Cell Transplantation, (2001) Vol. 10, No. 4-5, pp. 473-477. print.  
ISSN: 0963-6897.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 3 Oct 2001  
Last Updated on STN: 23 Feb 2002

AB Pancreatic islet transplantation for patients with diabetes mellitus has been hindered by the problem of donor shortage, as is the case for transplantation of other organs. Among several measures to overcome this problem, cell

transplantation using xenogenic cell lines has been considered. For the treatment of diabetic patients, a murine pancreatic beta-cell line MIN6 is a potential source of cell transplant. In order to restrict otherwise unlimited proliferation of transplanted MIN6 cells, cells are rendered to form spheroidal aggregates (SMIN6) on nonadherent culture dishes. SMIN6 stopped its growth around day 7 with a diameter of 220 +/- 40 µm and kept its size almost constant at least until day 28. SMIN6 cells, however, had reduced responsiveness of insulin secretion to glucose concentration compared with MIN6 cells cultured in a monolayer. On the other hand, spheroid MIN6 cells formed in the presence of extracellular matrix gel (SMIN6E) possessed the capacity for glucose-dependent insulin secretion comparable with conventional MIN6 cells. SMIN6E encapsulated in agarose beads (SMIN6E-B) was also viable for at least 1 month in vitro with a constant diameter and favorable glucose responsiveness. The development of spheroid-type MIN6 may contribute to the future clinical application of MIN6 or other beta-cell lines for treatment of diabetes mellitus.

L21 ANSWER 13 OF 41 EMBASE COPYRIGHT (c) 2010 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2001173091 EMBASE Full-text

TITLE: 3D bone tissue engineered with bioactive microspheres in simulated microgravity.

AUTHOR: Ayyaswamy, Portonovo S. (correspondence)

CORPORATE SOURCE: Department of Mechanical Engineering and Applied Mechanics, Center for Bioactive Materials and Tissue Engineering, University of Pennsylvania, Philadelphia, PA 19104, United States. ayya@seas.upenn.edu

AUTHOR: Ayyaswamy, Portonovo S. (correspondence)

CORPORATE SOURCE: Dept. of Bioengg. (Q.-Q. Q., P. D.), Ctr. for Bioactive Mat./Tissue Engg., University of Pennsylvania, Philadelphia, PA 19104, United States. ayya@seas.upenn.edu

SOURCE: In Vitro Cellular and Developmental Biology - Animal, (2001) Vol. 37, No. 3 I, pp. 157-165.

Refs: 10

ISSN: 1071-2690 CODEN: ICDBEO

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation

029 Clinical and Experimental Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 31 May 2001

Last Updated on STN: 31 May 2001

AB Three-dimensional (3D) osteoblast cell cultures were obtained in rotating-wall vessels (RWV), simulating microgravity. Three types of bioactive microcarriers, specifically modified bioactive glass particles, bioceramic hollow microspheres, and biodegradable bioactive glass-polymer composite microspheres, were developed and used with osteoblasts. The surfaces of composite microspheres fully transformed into bone apatite after 2-wk immersion in simulated physiological fluid, which demonstrated their bone-bonding ability. The motion of microcarriers in RWVs was photographically recorded and numerically analyzed. The trajectories of hollow microspheres showed that they migrated and eventually stayed around at the central region of the RWV. At their surfaces, shear stresses were low. In contrast, solid glass or polymer particles moved toward and finally bounced off the outer wall of the RWVs. Cell culture studies in the RWV using bone marrow stromal cells showed that the cells attached to and formed 3D aggregates with the hollow microspheres. Extracellular matrix and mineralization were observed in the

aggregates. Cell culture studies also confirmed the ability of the composite ~~microspheres~~ to support 3D bone-like tissue formation. These data suggest that the new hollow bioceramic ~~microspheres~~ and degradable composite ~~microspheres~~ can be used as microcarriers for 3D bone ~~tissue engineering~~ in microgravity. They also have potential applications as drug delivery systems.

L21 ANSWER 14 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2001:905513 HCAPLUS Full-text

DOCUMENT NUMBER: 136:131922

TITLE: Changes in the expression of annexin A5 gene during in vitro chondrocyte differentiation: influence of cell attachment

AUTHOR(S): Turnay, Javier; Olmo, Nieves; Lizarbe, M. Antonia; Von der Mark, Klaus

CORPORATE SOURCE: Department of Biochemistry and Molecular Biology I, Faculty of Chemistry, Complutense University, Madrid, 28040, Spain

SOURCE: Journal of Cellular Biochemistry (2001), 84(1), 132-142

CODEN: JCEBD5; ISSN: 0730-2312

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Several lines of evidence indicate that annexin A5, a membrane-associated protein with calcium-channel activity, plays a key role in cartilage calcification during endochondral ossification. As a major constituent of cartilage ~~matrix~~ vesicles, which are released from microvilli of hypertrophic chondrocytes, it is involved in calcium uptake necessary for the initial stages of cartilage calcification. Little is known, however, concerning transcriptional regulation of the annexin A5 gene during chondrocyte differentiation. Here, the authors report on changes in annexin A5 expression by measuring mRNA and protein levels during in vitro differentiation of chick sternal chondrocytes to the hypertrophic phenotype. Terminal differentiation of mature sternal chondrocytes was achieved in the presence of sodium ascorbate in high-d. cultures growing either in ~~monolayer~~ or over agarose as ~~cell aggregates~~. Differentiation of chondrocytes to hypertrophic cells was followed by morphol. anal. and by the onset of type X collagen expression. High expression levels of annexin A5 mRNA were detected in chondrocytes freshly isolated from the sterna by enzymic digestion and subsequently in cells growing in ~~monolayer~~, but annexin A5 gene transcription was rapidly downregulated when cells were grown in suspension as aggregates over agarose. However, protein levels did not decrease probably due to its low turnover rate. In suspension culture, annexin A5 mRNA reappeared after 3 wk concomitantly with segregation of the aggregates into ~~single cells~~ and onset of chondrocyte hypertrophy. The downregulation of annexin A5 expression in cells growing as ~~matrix~~-rich aggregates was reverted when extracellular ~~matrix~~ components were removed and cells were reseeded onto tissue culture plastic, suggesting that cell spreading, formation of focal contacts and stress fibers stimulated annexin A5 expression in proliferating as well as in hypertrophic chondrocytes. OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD

(3 CITINGS)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 15 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2000:370621 HCAPLUS Full-text

DOCUMENT NUMBER: 133:264864

TITLE: Expression of an activated Notch4(int-3) oncoprotein disrupts morphogenesis and induces an invasive phenotype in mammary epithelial cells in vitro

AUTHOR(S): Soriano, Jesus V.; Uyttendaele, Hendrik; Kitajewski, Jan; Montesano, Roberto  
 CORPORATE SOURCE: Institute of Histology and Embryology, Department of Morphology, University of Geneva Medical Center, Geneva, CH-1211/4, Switz.  
 SOURCE: International Journal of Cancer (2000), 86(5), 652-659  
 CODEN: IJCNAW; ISSN: 0020-7136  
 PUBLISHER: Wiley-Liss, Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The protein encoded by the Notch4 gene is a member of the Notch/lin-12 family of transmembrane receptor proteins, which were shown to control cell fate determination and cell differentiation in a wide variety of organisms. Expression of Notch4(int-3), a truncated form of Notch4 having most of its extracellular domain deleted, as a transgene in mice induces the formation of poorly differentiated mammary carcinomas. To establish whether Notch4(int-3) has the capacity of subverting normal epithelial architecture, the authors assessed the effect of Notch4(int-3) expression on the in vitro morphogenetic properties of TAC-2 mammary epithelial cells. When growth in 3 -dimensional collagen gels in the presence of hydrocortisone, both wild-type and LacZ-transfected TAC-2 cells formed alveolar-like structures composed of polarized epithelial cells surrounding a central lumen. In contrast, TAC-2 cells programmed to express Notch4(int-3) formed compact cell aggregates devoid of tissue-specific organization. In addition, when grown on the surface of a collagen gel, Notch4(int-3)-expressing TAC-2 cells invaded the underlying matrix, whereas TAC-2 LacZ cells remained strictly confined to the gel surface. Expression of Notch4(int-3) in TAC-2 cells also disrupted contact-inhibition of cell proliferation, resulting in cell multilayering. These results suggest that the ability of Notch4(int-3) to subvert normal epithelial morphogenesis and to promote invasion of the extracellular matrix contributes significantly to its tumorigenic potential. OS.CITING REF COUNT: 39 THERE ARE 39 CAPLUS RECORDS THAT CITE THIS

RECORD (40 CITINGS)  
 REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 16 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2000:535994 HCAPLUS Full-text  
 DOCUMENT NUMBER: 133:236911  
 TITLE: Mechanochemical manipulation of hepatocyte aggregation can selectively induce or repress liver-specific function  
 AUTHOR(S): Semler, Eric J.; Ranucci, Colette S.; Moghe, Prabhas V.  
 CORPORATE SOURCE: Department of Chemical and Biochemical Engineering, Rutgers University, Piscataway, NJ, 08854, USA  
 SOURCE: Biotechnology and Bioengineering (2000), 69(4), 359-369  
 CODEN: BIBIAU; ISSN: 0006-3592  
 PUBLISHER: John Wiley & Sons, Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Controlled activation of hepatocyte aggregation is critical to three -dimensional (3D) multicellular morphogenesis during native regeneration of liver as well as tissue reconstruction therapies. In this work, we quantify the stimulatory effects of two model hepatotrophic activators, epidermal growth factor (EGF) and hepatocyte growth factor (HGF), on the aggregation kinetics and liver-specific function of hepatocytes cultured on organotypic substrates with differing mech. resistivity. Substrate-specific morphogenesis of cultured hepatocytes is induced on a tissue basement membrane extract, Matrigel, formulated at two distinct levels

of mech. compliance (storage modulus  $G'$ , at oscillatory shear rate 1 rad/s, was 34 Pa for basal Matrigel and 118 Pa for crosslinked Matrigel). Overall, we report that growth factor stimulation selectively promotes the kinetics of aggregation in the form of two-dimensional corded aggregates on basal Matrigel and three-dimensional spheroidal aggregates on crosslinked Matrigel. Our anal. also indicates that co-stimulation with EGF and HGF (20 ng/mL each) cooperatively maximizes the kinetics of aggregation in a substrate-specific manner. In addition, we show that the role of growth factor stimulation on hepatocyte function is sensitively governed by the mech. compliance of the substrate. In particular, on ~~matrixes~~ with high compliance, co-stimulatory aggregation is shown to elicit a marked increase in albumin secretion rate, whereas on ~~matrixes~~ with low compliance aggregation results in effective functional repression to basal, unstimulated levels. Thus, our studies highlight a novel interplay of physicochem. parameters of the culture microenvironment, leading to selective enhancement or repression of differentiated functions of hepatocytes, in concert with the activation of cellular morphogenesis. OS.CITING REF COUNT: 45 THERE ARE 45 CAPLUS RECORDS THAT CITE THIS

REFERENCE COUNT: 39 RECORD (45 CITINGS)  
THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 17 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2000:685502 HCAPLUS Full-text

DOCUMENT NUMBER: 133:347596

TITLE: The roles of ~~matrix~~ molecules in mediating  
chondrocyte aggregation, attachment, and spreading

AUTHOR(S): Lee, Vivian; Cao, Liu; Zhang, Yaou; Kiani, Chris;  
Adams, Mark E.; Yang, Burton B.

CORPORATE SOURCE: Sunnybrook & Women's College Health Sciences Centre  
and Department of Laboratory Medicine and  
Pathobiology, University of Toronto, Toronto, ON, Can.

SOURCE: Journal of Cellular Biochemistry (2000),  
79(2), 322-333

CODEN: JCEBD5; ISSN: 0730-2312

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The most abundant macromols. in cartilage are hyaluronan, collagen, aggrecan, and link protein, which are believed to play roles in maintaining a unique ~~three-dimensional~~ network for a functional joint. This study was designed to investigate the roles of the major extracellular mols. in mediating chondrocyte-~~matrix~~ interactions. The authors employed specific approaches to remove components individually or in combination: hyaluronan was digested with hyaluronidase; type II collagen was digested with collagenase; aggrecan expression was inhibited with antisense and  $\beta$ -xyloside approaches; and link protein expression was inhibited with antisense oligonucleotides. Digestion of hyaluronan induced chondrocyte attachment to tissue culture plates, collagen-coated plates, and ~~fibroblast~~-like chondrocyte cultures, and induced chondrocyte aggregation. Treated chondrocytes exhibited a ~~fibroblast~~-like morphol., and the effects of hyaluronidase were dose-dependent. Conversely, the effect of collagenase on chondrocyte adhesion and aggregation was far less pronounced. Treatment with Arg-Gly-Asp peptide inhibited chondrocyte-collagen interaction. Chondrocyte attachment was enhanced by antisense oligonucleotides complementary to aggrecan and link protein and by  $\beta$ -xyloside treatment. Nevertheless, hyaluronan seems to predominate over the other mols. in mediating chondrocyte-~~matrix~~ interactions.

OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS  
RECORD (13 CITINGS)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 18 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1999:223865 HCAPLUS Full-text

DOCUMENT NUMBER: 131:14441

TITLE: Anti-apoptotic signaling of the IGF-I receptor in fibroblasts following loss of matrix adhesion

AUTHOR(S): Valentinis, Barbara; Morrione, Andrea; Peruzzi, Francesca; Prisco, Marco; Reiss, Krzysztof; Baserga, Renato

CORPORATE SOURCE: Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA, 19107, USA

SOURCE: Oncogene (1999), 18(10), 1827-1836

CODEN: ONCNES; ISSN: 0950-9232

PUBLISHER: Stockton Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The type 1 insulin-like growth factor receptor (IGF-IR) is known to protect cells from a variety of apoptotic injuries. In several instances, the anti-apoptotic effect of the wild type IGF-IR is more evident under conditions of anchorage-independence than in cells in ~~monolayer~~ cultures. We have investigated IGF-IR signaling in cells in anoikis, a form of apoptosis that occurs when cells are denied attachment to the extracellular matrix. IGF-I protects mouse embryo fibroblasts (MEF) from anoikis caused by withdrawal of growth factors. Survival is dependent on the concentration of IGF-I and a sufficient number of functional IGF-I receptors. In this model, IGF-I protection correlates best with ras activation and cell-to-cell aggregation, while phosphatidylinositol 3-kinase, Akt and MAP kinases seem to play a lesser, alternative role. OS.CITING REF COUNT: 63 THERE ARE 63 CAPLUS RECORDS THAT CITE THIS

RECORD (63 CITINGS)

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 19 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2000:46306 HCAPLUS Full-text

DOCUMENT NUMBER: 132:227382

TITLE: Enhanced cell aggregation and liver functions using polymers modified with a cell-specific ligand in primary hepatocyte cultures

AUTHOR(S): Yamada, Keisuke; Kamihira, Masamichi; Iijima, Shinji

CORPORATE SOURCE: Department of Biotechnology, Graduate School of Engineering, Nagoya University, Nagoya, 464-8603, Japan

SOURCE: Journal of Bioscience and Bioengineering (1999), 88(5), 557-562

CODEN: JBBIF6; ISSN: 1389-1723

PUBLISHER: Society for Bioscience and Bioengineering, Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hepatocytes cultured as multicellular aggregates called ~~spheroids~~ exhibit enhanced liver functions and maintain them over a long period compared with ~~monolayer~~ culture. We previously reported the induction of hepatocyte ~~spheroids~~ using the synthetic polymer Eudragit (a copolymer of methacrylic acid and methyl-methacrylate) as an artificial matrix in a cell suspension system. In this method, hepatocyte aggregation was promoted by the effects of electrostatic and hydrophobic interactions between cells and the polymer. To enhance the cell aggregation ability and cell-specificity of the polymer, in the present study, we prepared hepatocyte-targeting polymers containing lactone, a ligand of the asialoglycoprotein receptor. Addition of the lactone-modified polymers to the medium promoted cell aggregation and spheroid formation more effectively than unmodified Eudragit. The ~~spheroids~~ induced by the polymers exhibited enhanced



liver functions, i.e., albumin secretion, ammonia removal, and urea synthesis, from early in the culture. We also investigated the induction of hetero-spheroids composed of various liver constitutive cells by this method. The hetero-spheroids induced by the polymers showed improved liver functions. OS.CITING REF COUNT: 8  
THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD

(8 CITINGS)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 20 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1999:807717 HCAPLUS Full-text

DOCUMENT NUMBER: 132:178461

TITLE: In situ hybridization study of type I, II, X collagens and aggrecan mRNAs in the developing condylar cartilage of fetal mouse mandible

AUTHOR(S): Fukada, Kenji; Shibata, Shunichi; Suzuki, Shoichi; Ohya, Keiichi; Kuroda, Takayuki

CORPORATE SOURCE: 2nd Department of Orthodontics, Department of Dental Pharmacology, School of Dentistry, Tokyo Medical and Dental University, Tokyo, 113-8549, Japan

SOURCE: Journal of Anatomy (1999), 195(3), 321-329

CODEN: JOANAY; ISSN: 0021-8782

PUBLISHER: Cambridge University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The aim of this study was to investigate the developmental characteristics of the mandibular condyle in sequential phases at the gene level using in situ hybridization. At d 14.5 of gestation, although no expression of type II collagen mRNA was observed, aggrecan mRNA was detected with type I collagen mRNA in the posterior region of the mesenchymal cell aggregation continuous with the ossifying mandibular bone anlage prior to chondrogenesis. At d 15.0 of gestation, the first cartilaginous tissue appeared at the posterior edge of the ossifying mandibular bone anlage. The primarily formed chondrocytes in the cartilage matrix had already shown the appearance of hypertrophy and expressed types I, II and X collagens and aggrecan mRNAs simultaneously. At d 16.0 of gestation, the condylar cartilage increased in size due to accumulation of hypertrophic chondrocytes characterized by the expression of type X collagen mRNA, whereas the expression of type I collagen mRNA had been reduced in the hypertrophic chondrocytes and was confined to the periosteal osteogenic cells surrounding the cartilaginous tissue. At d 18.0 of gestation before birth, cartilage-characteristic gene expression had been reduced in the chondrocytes of the lower half of the hypertrophic cell layer. The present findings demonstrate that the initial chondrogenesis for the mandibular condyle starts continuous with the posterior edge of the mandibular periosteum and that chondroprogenitor cells for the condylar cartilage rapidly differentiate into hypertrophic chondrocytes. Further, it is indicated that sequential rapid changes and redns. of each mRNA might be closely related to the construction of the temporal mandibular ramus in the fetal stage. OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS

RECORD (18 CITINGS)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 21 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1999:617396 HCAPLUS Full-text

TITLE: Use of 3-D growth to develop tissuelike spheroids and bilayers as prostate cancer cell models.

AUTHOR(S): Enmon, Richard Jr.; O'Connor, Kim; Lacks, Daniel; Schwartz, Daniel; Clejan, Sanda

CORPORATE SOURCE: Chemical Engineering and Molecular & Cellular Biology,

SOURCE: Tulane University, New Orleans, LA, 70118, USA  
 Book of Abstracts, 218th ACS National Meeting, New Orleans, Aug. 22-26 (1999), MEDI-025.  
 American Chemical Society: Washington, D. C.  
 CODEN: 67ZJA5

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Prostate cancer is the most commonly diagnosed cancer in American men. Currently, there is no cure for this disease when it has metastasized and become hormone-refractory. Through the use of three-dimensional cell growth, we have developed two models of DU 145 human prostate carcinoma cells to be used to help understand the mol. basis of metastases in hormone-refractory prostate cancer. One model is tissue-like spheroids cultivated in the NASA High Aspect Rotating-Wall Vessel; the other is a cellular bilayer grown on a two-dimensional substratum in Transwell inserts. The NASA vessel provides a quiescent environment in which DU 145 cells grow suspended in culture medium to form spherical cell aggregates. We have done extensive characterization of the spheroids and bilayer. Specifically, we have examined cell growth in terms of doubling time and cell cycle, morphol., cytoskeletal proteins, autocrine growth factors and their receptors, and the extracellular matrix. All data to date suggests that the tissue-like spheroids behave as well differentiated solid tumors and the bilayer as an aggressive invading tumor margin. For example, staining intensity for two biomarkers of differentiation, cytokeratin 8 and 18, is a factor of 3 times greater for the spheroids than for the bilayer. We have attributed differences in the two cell models to increased three-dimensional growth in the spheroids which results in greater cell-cell and cell-matrix interactions as well as the formation of a rich interstitial fluid containing growth factors and other biol. effectors.

L21 ANSWER 22 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1999:36628 HCAPLUS Full-text

DOCUMENT NUMBER: 130:194915

TITLE: Chondrocyte differentiation in a rat  
 mesenchymal cell line

AUTHOR(S): Lunstrum, Gregory P.; Keene, Douglas R.; Weksler, Nicole B.; Cho, Yoon-Jae; Cornwall, Marcus; Horton, William A.

CORPORATE SOURCE: Research Department, Shriners Hospital for Children, Portland, OR, 97201, USA

SOURCE: Journal of Histochemistry and Cytochemistry (1999), 47(1), 1-6

CODEN: JHCYAS; ISSN: 0022-1554

PUBLISHER: Histochemical Society, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A combination of morphol. and histochem. methods to was used demonstrate that rat calvaria-derived mesenchymal cells (RCJ 3.1C5.18) in culture progress through the differentiation pathway exhibited by chondrocytes in the endochondral growth plate. The cells were grown either as monolayer or suspension cultures. Subconfluent monolayer cultures did not express markers typical of chondrocyte phenotypes. However, after reaching confluency the cells formed nodules of chondrocytic cells separated by cartilage-appearing matrix and encapsulated by fibroblast-like cells. Suspension culture produced cell aggregates with similar characteristics. Matrix in both the nodules and aggregates stained for collagen types II and XI and aggrecan, and some cells displayed a distinctive pericellular matrix that stained for type X collagen. Mineralization was evident in older cultures. By electron microscopy, most cells in the aggregates appeared as typical chondrocytes. However, some larger cells were surrounded by a "mat" of matrix comprised of hexagonal arrays of dense nodules interconnected by a filamentous

network. Immunogold localization confirmed the presence of collagen type X in this ~~matrix~~. Anal. of markers of chondrocyte differentiation and terminal differentiation over time showed that these markers were acquired sequentially over 2 wk of culture. This model system will be useful to study the regulation of various steps in the chondrocyte differentiation pathway. OS.CITING REF COUNT: 37 THERE ARE 37 CAPLUS RECORDS THAT CITE THIS

RECORD (37 CITINGS)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 23 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1998:383053 HCAPLUS Full-text

DOCUMENT NUMBER: 129:107324

ORIGINAL REFERENCE NO.: 129:22016h,22017a

TITLE: Induction of ~~matrix~~ metalloproteinase-9 requires a polymerized actin cytoskeleton in human malignant glioma cells

AUTHOR(S): Chintala, Shravan K.; Sawaya, Raymond; Aggarwal, Bharat B.; Majumder, Sadhan; Giri, Dipak K.; Kyritsis, Athanassios P.; Gokaslan, Ziya L.; Rao, Jasti S.

CORPORATE SOURCE: Department of Neurosurgery, Cytokine Research Laboratory, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA

SOURCE: Journal of Biological Chemistry (1998), 273(22), 13545-13551

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Alterations in cytoskeleton and subsequent cell shape changes exert specific effects on the expression of various genes. The authors' previous results suggested that malignant human gliomas express elevated levels of ~~matrix~~ metalloproteinases compared with normal brain tissue and low grade gliomas. To understand the role of cell shape changes on ~~matrix~~ metalloproteinase expression in human glioma cells, the authors treated SNB19 cells with cytochalasin-D, an inhibitor of actin polymerization, and colchicine-B, a tubulin inhibitor, in the presence of phorbol 12-myristate 13-acetate. Cytochalasin-D treatment of SNB19 cells resulted in the loss of phorbol 12-myristate 13-acetate-induced ~~matrix~~ metalloproteinase-9 (also known as ~~gelatinase-B~~) expression and coincided with inhibition of actin polymerization, resulting in cell rounding. Moreover, compared with ~~monolayers~~, cells grown as ~~spheroids~~ or cell aggregates failed to express ~~matrix~~ metalloproteinase-9 in the presence of phorbol 12-myristate 13-acetate. ~~Matrix~~ metalloproteinase-9 expression was also inhibited by calphostin-C, a protein kinase inhibitor, suggesting the involvement of protein kinase C in ~~matrix~~ metalloproteinase-9 expression. Phorbol 12-myristate 13-acetate-induced invasion of SNB19 cells through Matrigel was inhibited by cytochalasin-D and calphostin-C. These results suggest that the actin polymerization transduces signals that modulate the expression of ~~matrix~~ metalloproteinase-9 expression and the subsequent invasion of human glioma cells.

OS.CITING REF COUNT: 45 THERE ARE 45 CAPLUS RECORDS THAT CITE THIS RECORD (45 CITINGS)

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 24 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1998:507774 HCAPLUS Full-text

DOCUMENT NUMBER: 129:221168

ORIGINAL REFERENCE NO.: 129:44865a,44868a

TITLE: Efficient induction of hepatocyte ~~spheroids~~

in a suspension culture using a water-soluble synthetic polymer as an artificial matrix

AUTHOR(S): Yamada, Keisuke; Kamihira, Masamichi; Hamamoto, Ryuji; Iijima, Shinji

CORPORATE SOURCE: Department of Biotechnology, Graduate School of Engineering, Nagoya University, Nagoya, 464-8603, Japan

SOURCE: Journal of Biochemistry (1998), 123(6), 1017-1023  
CODEN: JOBIAO; ISSN: 0021-924X

PUBLISHER: Japanese Biochemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The preparation of hepatocyte spheroids by adding a water-soluble synthetic polymer as an artificial matrix was performed in a cell suspension system. Cell-aggregation was promoted without cytotoxicity by adding Eudragit (a copolymer of methacrylic acid and methylmethacrylate) to the culture medium. Spheroid-like cell aggregates, whose liver functions were enhanced, were effectively formed in the presence of 0.1% Eudragit, independent of the cultural substratum. Moreover, the mass preparation of spheroids could be achieved with a high production yield by means of a suspension culture in a spinner flask. In this case, the polymer protected the cells from damage due to agitation. The spheroids induced with Eudragit expressed high liver functions, such as albumin secretion, ammonia removal, and urea synthesis. On histol. observation, the spheroids showed a well-developed cell adhesion apparatus and bile canaliculi. In addition, a higher calcium ion concentration in the cells of spheroids was observed compared with in monolayer cells. OS.CITING REF COUNT: 32 THERE ARE 32 CAPLUS RECORDS THAT CITE THIS

RECORD (32 CITINGS)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 25 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1999:39096 HCAPLUS Full-text

DOCUMENT NUMBER: 130:194930

TITLE: Differentiation and proliferation of primary rat hepatocytes cultured as spheroids

AUTHOR(S): Hamamoto, Ryuji; Yamada, Keisuke; Kamihira, Masamichi; Iijima, Shinji

CORPORATE SOURCE: Department of Biotechnology, Graduate School of Engineering, Nagoya University, Nagoya, 464-8603, Japan

SOURCE: Journal of Biochemistry (1998), 124(5), 972-979

CODEN: JOBIAO; ISSN: 0021-924X

PUBLISHER: Japanese Biochemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We studied spheroid (multicellular aggregate) formation by hepatocytes and the expression of liver-specific functions such as albumin secretion when hepatocytes were cultured with various extracellular matrixes. Hepatocytes cultured on Primaria and poly-D-lysine coated dishes, and in the presence of a polymer, Eudragit, formed spheroids, and they also exhibited higher liver-specific functions and poor growth compared to monolayer cultures. The results indicated that the cell morphol. change and cell-cell interaction caused by the spheroid formation were key factors promoting the expression of the liver-specific functions. To elucidate the mechanism underlying the poor growth in spheroids, we examined the HGF signaling pathway. Phosphorylation and down-regulation of the HGF receptor (c-Met proto-oncogene product) were observed for the cells from both monolayer and spheroid cultures, but Ras activation was partly blocked in

spheroids. Furthermore, we found that CDK inhibitors, p21 and p27, were highly expressed in spheroids. These results suggested that the reduced Ras signaling and high expression of the CDK inhibitors might cause the lower growth in spheroids. We then examined the relationship between liver-enriched transcription factors (C/EBP $\alpha$  and  $\beta$ ) and liver-specific functions. The results revealed that the high expression of C/EBP $\alpha$  was maintained during cultures when hepatocytes formed spheroids.

Antisense oligonucleotides of C/EBP $\alpha$  repressed albumin secretion and the expression of p21, suggesting that the transcription factor, C/EBP $\alpha$ , may play a crucial role in the growth and differentiation of hepatocytes in spheroids.

OS.CITING REF COUNT: 36 THERE ARE 36 CAPLUS RECORDS THAT CITE THIS RECORD (36 CITINGS)  
 REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 26 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1998:155842 HCAPLUS Full-text

DOCUMENT NUMBER: 128:281248

ORIGINAL REFERENCE NO.: 128:55648h,55649a

TITLE: Stimulation of extracellular matrix components in the normal brain by invading glioma cells

AUTHOR(S): Knott, Jo C. A.; Mahesparan, Rupavathana; Garcia-Cabrera, Inmaculada; Tysnes, Berit Bolge; Edvardsen, Klaus; Ness, Gro Oddveig; Mork, Sverre; Lund-Johansen, Morten; Bjerkvig, Rolf

CORPORATE SOURCE: Department of Anatomy and Cell Biology, University of Bergen, Bergen, Norway

SOURCE: International Journal of Cancer (1998), 75(6), 864-872

CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Malignant gliomas are characterized by an extensive invasion of tumor cells into the normal brain parenchyma. A substantial amount of data indicates that cell movement in general is regulated by specific interactions between extracellular matrix components and specific cell-surface receptors. In the present work, multicellular spheroids from 4 human glioma cell lines (U-373Mg, A-172Mg, U-251Mg and HF-66) were confronted with normal rat brain cell aggregates in vitro, which resulted in a progressive invasion of tumor cells into the brain aggregates. The co-cultures were then sectioned and immuno-stained for specific extracellular matrix components (laminin, fibronectin and collagen type IV) and for specific cell-surface receptors which bind to these components (integrins  $\beta$ 1,  $\beta$ 4,  $\alpha$ 3,  $\alpha$ 6). In addition, flow-cytometric measurements and Northern blot analyses showed expression of several different integrins within the cell lines. The  $\alpha$ 3 subunit was expressed strongly in all cell lines. Whereas the  $\beta$ 1 subunit was expressed weakly in exponentially growing monolayer cultures, it showed a pronounced expression in multicellular spheroids, indicating that the integrin expression may vary depending on the micro-environment within a tumor. Furthermore, normal brain tissue was able to produce laminin when confronted with the glioma cells, which also was observed for fibronectin and collagen type IV. The relevance of these observations to the in vivo situation was investigated further by immuno-staining 5 human glioma biopsy samples for laminin. In some areas of the tumors, specific deposits of laminin were observed. Thus, normal brain tissue has the ability to produce extracellular matrix components, such as laminin, collagen type IV and fibronectin, when confronted with invading glioma cells. The glioma cells express specific integrins which can interact with these extracellular matrix components. Such interactions may facilitate tumor cell migration and invasion. OS.CITING REF COUNT: 32 THERE ARE 32 CAPLUS RECORDS THAT CITE THIS

RECORD (32 CITINGS)

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 27 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1998:792757 HCAPLUS Full-text

DOCUMENT NUMBER: 130:166108

TITLE: Interactions of elastin fibers with  
fibroblasts a time-lapse cinemicrographic  
study

AUTHOR(S): Groult, V.; Hornebeck, W.; Robert, L.; Pouchelet, M.;  
Jacob, M. P.

CORPORATE SOURCE: INSERM U460, Paris, 75870, Fr.

SOURCE: Pathologie Biologie (1998), 46(7), 507-516

CODEN: PTBIAN; ISSN: 0031-3009

PUBLISHER: Expansion Scientifique Publications

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Adhesion of cells to the extracellular ~~matrix~~ is mediated by structural glycoproteins such as fibronectin and laminin, and also elastonectin, whose role is to ensure binding of elastin fibers to cells. Interactions between elastin fibers and human skin fibroblasts cultured in a Rose chamber were investigated by using cinemicrog. to observe elastin fiber attachment, detachment, and displacement over a five-day period. Elastin fiber displacement over the cell layer resulted in aggregation, which was measured using morphometry. The total number of isolated elastin fibers or aggregates decreased between 1h and 8h and remained stable thereafter. During the same time interval, significant decreases occurred in the nos. of isolated fibers and small aggregates (perimeter<0.268 mm; surface area<894  $\mu\text{m}^2$ ), whereas larger aggregates were formed. After 15 h of interaction, none of the aggregates had a perimeter greater than 0.536 mm, consistent with an increase in aggregate compacting. These data demonstrate that elastin-cell interactions do not occur at random. These interactions may play a pivotal role in morphogenesis and in maintaining the integrity of elastic tissues such as the arterial wall, lungs, and skin. OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD

(3 CITINGS)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 28 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1998:393102 HCAPLUS Full-text

DOCUMENT NUMBER: 129:92501

ORIGINAL REFERENCE NO.: 129:18995a,18998a

TITLE: Effects of polyelectrolyte complex (PEC) on human  
periodontal ligament fibroblast (HPLF)  
function. I. Three-dimensional  
structure of HPLF cultured on PEC

AUTHOR(S): Hamano, Takaichi; Teramoto, Akira; Iizuka, Eisaku;  
Abe, Koji

CORPORATE SOURCE: Department of Functional Polymer Science, Faculty of  
Textile Science and Technology, Shinshu University,  
Ueda, 386 8567, Japan

SOURCE: Journal of Biomedical Materials Research (1998  
, 41(2), 257-269

CODEN: JBMRBG; ISSN: 0021-9304

PUBLISHER: John Wiley &amp; Sons, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human periodontal ligament fibroblast (HPLF) cultured on tissue culture dishes (TCD), irresp. of the presence of serum, showed only a spreading form. In

contrast, using PEC as a ~~matrix~~, HPLF showed spreading, round, and aggregate forms. Cells of the inner part of the aggregate contacted with each other to form a 3-dimensional structure, and this condition corresponded to typical tissues in vivo. These seemed to be related to the interrelation between growth and morphol.; i.e., the HPLF of the spreading form was considered to belong to a proliferation phase, and the HPLF of the round and aggregate forms, with a little growth, seemed to belong to a functional phase of the cell cycle, indicating that PEC is able to control such cell functions as proliferation, morphol., and differentiation. The ~~cell aggregate~~ was observed only on PEC with carboxymethyl residues and was stained by alizarin red (AR), which suggested mineralization. The spreading cells on PEC containing sulfate residues were not stained by AR. Therefore, there was a certain relationship between cell growth and morphol., and that PEC affected the cell cycle and promoted proliferation and differentiation of HPLF.

OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)  
 REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 29 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1999:302389 HCAPLUS Full-text

DOCUMENT NUMBER: 131:115389

TITLE: Growth and differentiation of osteoblasts on hollow biocompatible ceramic microcarriers under microgravity conditions

AUTHOR(S): Qiu, Qing-Qing; Ducheyne, Paul; Ayyaswamy, Portonovo S.

CORPORATE SOURCE: Department of Bioengineering, University of Pennsylvania, Philadelphia, PA, 19104, USA

SOURCE: HTD (American Society of Mechanical Engineers) (1998), 362(Advances in Heat and Mass Transfer in Biotechnology, 1998), 49-53  
 CODEN: ASMHD8; ISSN: 0272-5673

PUBLISHER: American Society of Mechanical Engineers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In our recent studies with osteoblasts in the simulated microgravity environment of rotating-wall vessels (RWVs), we have observed the formation of ~~cell aggregates~~ and glass surface layers. In those studies, surface modified bioactive glass particles were employed as microcarriers. The growth and coverage of cells on the glass microcarriers were observed to be limited. We have also studied this problem from a numerical modeling viewpoint. Our numerical anal. of the particle dynamics in RWVs has revealed that the limited coverage noted in the expts. may be attributable to both the high shear stress imparted to the particle surface and the collisions experienced by the microcarrier with the outer wall of the vessel. The high shear stress and wall collisions arise primarily as a result of the high d. of the microcarrier material. Here, we report the development of novel hollow bioceramic microspheres with an apparent d. in the range 0.8 .apprx. 1.0 g/cm<sup>3</sup>. These microcarriers alleviate the aforementioned problems. The hollow ceramic microspheres have an inner shell with composition of 58-72% SiO<sub>2</sub>, 28-42% Al<sub>2</sub>O<sub>3</sub> (in % by weight) and a porous calcium phosphate surface. This surface was deposited using a fine particle sedimentation method. The hollow microspheres were sintered at 800°C for 1h. FTIR anal. indicated that crystalline calcium hydroxyapatite (HA) was present in the porous surface. Particle trajectory analyses in both an inertial frame and a rotating frame have shown that these microspheres remain suspended in the RWV environment during the entire cell culture period without experiencing collisions with the outer wall of the vessel. Furthermore, the shear stress imparted on the microsphere surface is low (.apprx. 0.6 dyn/cm<sup>2</sup>). Our cell culture studies in the HARV employing the hollow microcarriers have shown that osteoblastic cells form 3-D aggregates. Extensive extracellular ~~matrix~~ and mineralization were also observed in these aggregates. OS.CITING REF COUNT: 1

THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD

(1 CITINGS)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 30 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1997:408821 HCAPLUS Full-text

DOCUMENT NUMBER: 127:107723

ORIGINAL REFERENCE NO.: 127:20747a,20750a

TITLE: Influence of spatial configuration on the expression of carcinoembryonic antigen and mucin antigens in human bladder cancer

AUTHOR(S): Larue, Helene; Parent-Vaugeois, Carmen; Bergeron, Alain; Champetier, Serge; Fradet, Yves

CORPORATE SOURCE: Laboratoire d'Uro-Oncologie Experimentale, Centre de recherche de l'Hotel-Dieu de Quebec, QC, G1R 2J6, Can.

SOURCE: International Journal of Cancer (1997), 71(6), 986-992

CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss

DOCUMENT TYPE: Journal

LANGUAGE: English

AB CEA and cellular mucin antigens have been recognized as potential targets for specific immunotherapy and are frequently expressed in bladder cancer. We studied the coordinated expression of a bladder cancer-associated CEA glycoform and of the mucins MUC1, MUC2 and MAUB under various growth conditions in the MGH-U3 bladder-cancer cell line. CEA and MUC2 mRNAs and proteins were detected in nude mouse tumors and spheroids but not in monolayer cultures. Expression of MAUB and bladder-cancer CEA also was induced according to spatial configuration of cells. MUC1 was always expressed under various growth conditions, but its glycosylation was modulated: in spheroids and mostly in tumor cells, the SM3 protein epitope was unmasked and sialyl-Tn was induced. The kinetics of modulation of MAUB and bladder-cancer CEA were different. The epitope recognized by the monoclonal antibody (MAb) 19A211 was rapidly induced in the aggregation phase of spheroid formation and rapidly lost upon plating of tumor cells, suggesting a relationship with cell contact. By contrast, MAUB induction in spheroids was delayed to the compaction phase, when cell aggregates become resistant to disruption, and loss of expression upon tumor plating occurred slowly over several culture passages. No induction of these 2 antigens was observed in the presence of differentiation agents, endothelial cell products or interferon- $\gamma$ , but it occurred when MGH-U3 cells were cultured at high d. on extracellular matrix. Our results suggest that CEA and mucin antigen expression in bladder cancer is modulated by the spatial configuration of cells. OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD

(5 CITINGS)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 31 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1997:539914 HCAPLUS Full-text

TITLE: The deep cold biosphere: facts and hypothesis

AUTHOR(S): Vorobyova, Elena; Soina, Vera; Gorlenko, Michael; Minkovskaya, Natalia; Zalinova, Natalia; Mamukelashvili, Anzhelika; Gilichinsky, David; Rivkina, Elizaveta; Vishnivetskaya, Tatiana

CORPORATE SOURCE: Department of Soil Biology, Moscow State University, Moscow, 119899, Russia

SOURCE: FEMS Microbiology Reviews (1997), 20(3-4), 277-290



CODEN: FMREE4; ISSN: 0168-6445

PUBLISHER: Elsevier  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Deep subterranean ~~layers~~ may be regarded as the most stable environment for microorganisms where possible fluctuations should be explained by geol. events only. The anal. of the total amount of microorganisms has revealed that in sedimentary deposits their number is only one order of magnitude lower than the same parameter in soil. Taking into account the depth of sediments the microbial biomass in subterranean rocks has to be considerably larger than that in soils. Permafrost is the most constant and stable environment among deep habitats. Microbial communities survive in permafrost for at least some millions of years. The diversity of organisms and of microbial activities after permafrost thawing displays distinct differences to those in soils. The abundance of the bacterial biomass assumed is comparable in frozen and unfrozen sediments. Therefore, the permanently low temperature in permafrost is a stabilizing factor that sustains life in deep cold biotopes. Studies of microbial communities in permafrost sediments of different lithol. and age suggest that the level of subzero temperature and the duration of its influence define the ratio between the hypometabolic cells, readily reversible to proliferation, and the so-called viable but non-culturable cells (deep resting cells). To a certain extent, ~~cell~~ aggregates in the extracellular ~~matrix~~ may be regarded as an addnl. survival mechanism supporting the hypometabolic state of cells. There is indirect evidence for adaptive physiol. and biochem. processes in microorganisms during the long-term impact of cold. OS.CITING REF COUNT: 79 THERE ARE 79 CAPLUS RECORDS THAT CITE THIS

RECORD (79 CITINGS)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 32 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1996:532553 HCAPLUS Full-text

DOCUMENT NUMBER: 125:217791

ORIGINAL REFERENCE NO.: 125:40631a, 40634a

TITLE: PC12 ~~cell~~ aggregation and neurite growth in gels of collagen, laminin and fibronectin

AUTHOR(S): Baldwin, Samuel P.; Krewson, Christine E.; Saltzman, W. Mark

CORPORATE SOURCE: Department Chemical Engineering, Johns Hopkins University, Baltimore, MD, 21218, USA

SOURCE: International Journal of Developmental Neuroscience ( 1996), 14(3), 351-364  
CODEN: IJDND6; ISSN: 0736-5748

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB PC12 cells form aggregates when suspended within ~~three-~~ dimensional, self-assembled, type I collagen gels; these aggregates increase in size over time. In addition, when the cells are cultured in the presence of nerve growth factor, they express neurites, which extend through the ~~three-dimensional~~ matrix. In this report, the roles of fibronectin, laminin and nerve growth factor in PC12 ~~cell~~ aggregation and neurite growth following suspension in collagen ~~matrixes~~ were evaluated. ~~Single cells~~ and small clusters of cells were suspended in collagen gels; the kinetics of aggregation were determined by measurement of the projected area of each aggregate, and neurite lengths were determined by measurement of end-to-end distance. Fibronectin and laminin inhibited the aggregation of PC12 cells at 50 µg/mL, and fibronectin, but not laminin, inhibited the growth of neurites at 100 µg/mL. In the absence of serum, the aggregation of cells cultured with nerve growth factor was almost completely inhibited, but the average neurite length was

unaffected. In the presence of nerve growth factor, the extent of cell aggregation could not be explained simply by an increase in cell number, suggesting the presence of two sep. mechanisms for aggregate growth: one dependent on cell motility and another dependent on cell proliferation. OS.CITING REF COUNT: 28  
THERE ARE 28 CAPLUS RECORDS THAT CITE THIS

RECORD (28 CITINGS)

L21 ANSWER 33 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1996:381000 HCAPLUS Full-text

DOCUMENT NUMBER: 125:55020

ORIGINAL REFERENCE NO.: 125:10537a,10540a

TITLE: Effects of the carbohydrate-binding protein galectin-3 on the invasiveness of human breast carcinoma cells

AUTHOR(S): Le Marer, Nadia; Hughes, R. Colin

CORPORATE SOURCE: National Inst. Med. Res., London, NW7 1AA, UK

SOURCE: Journal of Cellular Physiology (1996), 168(1), 51-58

CODEN: JCLLAX; ISSN: 0021-9541

PUBLISHER: Wiley-Liss

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Galectin-3 is a Mr 30,000 protein with carbohydrate-binding specificity for type I and II ABH blood group epitopes and polylactosamine glycans expressed on cell surface and extracellular matrix glycoproteins such as laminin. Cell lines propagated from human normal mammary epithelia and from benign or infiltrating components of primary breast tumors express low levels of galectin-3 in the cytoplasm. However, galectin-3 when added exogenously in solution or when bound within a three-dimensional matrix markedly enhanced the migration of the primary tumor cell lines through a Matrigel barrier. Galectin-3 expression in the cytoplasm and intercellularly on surface membranes was greatly increased in cell lines propagated from malignant ascites and pleural effusions of late stage breast cancer. These cell lines were non-invasive in the Matrigel assay and exogenous galectin-3 had no enhancing effect on invasiveness. These results suggest that galectin-3 could play multiple roles in cell metastasis at an early invasive stage by acting in a paracrine manner to stimulate cell migration through an extracellular matrix, and in later stage cancers in synergy with other mediators of cell-cell aggregation. However, endogenous galectin-3 expression in human breast cancers is not correlated directly with their invasive potential in vitro.

OS.CITING REF COUNT: 55 THERE ARE 55 CAPLUS RECORDS THAT CITE THIS

RECORD (56 CITINGS)

L21 ANSWER 34 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1994:213735 HCAPLUS Full-text

DOCUMENT NUMBER: 120:213735

ORIGINAL REFERENCE NO.: 120:37817a,37820a

TITLE: Cell aggregation and neurite growth in gels of extracellular matrix molecules

AUTHOR(S): Krewson, Christine E.; Chung, Sonia W.; Dai, Weiguo; Saltzman, W. Mark

CORPORATE SOURCE: Dep. Chem. Eng., Johns Hopkins Univ., Baltimore, MD, 21218, USA

SOURCE: Biotechnology and Bioengineering (1994), 43(7), 555-62

CODEN: BIBIAU; ISSN: 0006-3592

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Components of the extracellular matrix are believed to guide both nerve cells and neurites to their targets during embryogenesis and, therefore, might be useful for controlling regeneration of nervous tissue in adults. To study the influence

of extracellular conditions on neurite outgrowth and cell motility, PC12 cells were suspended in ~~three- dimensional gels~~ containing (i) collagen (0.4 to 2 mg/mL), (ii) collagen (1 mg/mL) with added fibronectin or laminin (1 to 100 µg/mL), and (ii) agarose (7 mg/mL) with added collagen (0.001 to 1 mg/mL). Neurite outgrowth was stimulated with nerve growth factor (NGF) and both the extent of neurite outgrowth and cell aggregation were quantitated over 10 to 12 days in culture. The extent of neurite outgrowth was greatest at the lowest collagen concentration tested (0.4 mg/mL) and decreased with increasing concentration. The addition of laminin or fibronectin altered the extent of the neurite outgrowth in collagen ~~gels~~, but the differences were small. Although no neurite growth was observed in pure agarose ~~gels~~, considerable neurite outgrowth occurred with the addition of small amts.

(≥0.01 mg/mL) of collagen. Mean aggregate size increased more quickly in ~~gels~~ with lower concns. of collagen. For cells in 1.0 mg/mL collagen, a four- to fivefold increase in aggregate volume was seen between days 2 and 10 of the culture period, whereas the increase in DNA content during this same period was less than twofold, suggesting that the ~~cells~~ were aggregating, not multiplying. These results suggest that the composition of the ~~matrix~~ supporting nerve cells has a significant effect on both neurite outgrowth and cell motility. OS.CITING REF COUNT: 22 THERE ARE 22 CAPLUS RECORDS THAT CITE THIS

RECORD (22 CITINGS)

L21 ANSWER 35 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1993:479877 HCAPLUS Full-text

DOCUMENT NUMBER: 119:79877

ORIGINAL REFERENCE NO.: 119:14191a,14194a

TITLE: Cell community. Regulation of cell-substratum interaction for bioartificial organs

AUTHOR(S): Akaike, Toshihiro

CORPORATE SOURCE: Dep. Biomol. Eng., Tokyo Inst. Technol., Yokohama, 227, Japan

SOURCE: Tanpakushitsu Kakusan Koso (1993), 38(7), 1345-53

CODEN: TAKKAJ; ISSN: 0039-9450

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review, with 11 refs., on the construction of artificial organs from component natural cells by anal. and regulation of the interaction between cells, cell and ~~matrix~~, and cell and regulatory factors. Poly(N-p-vinylbenzyl-D-lactonamide) (PVLA) as a model for asialoglycoprotein for a biomimetic adhesion substrate material for liver ~~cells~~, and construction of ~~multi-layer cell aggregate~~ from a mixed culture of parenchymal and nonparenchymal liver cells on PVLA are also discussed.

L21 ANSWER 36 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1994:154138 HCAPLUS Full-text

DOCUMENT NUMBER: 120:154138

ORIGINAL REFERENCE NO.: 120:26913a,26916a

TITLE: Distribution of acidic and basic ~~fibroblast~~ growth factors in ovine skin during follicle morphogenesis

AUTHOR(S): du Cros, D. L.; Isaacs, K.; Moore, G. P. M.

CORPORATE SOURCE: Div. Anim. Prod., CSIRO, Prospect, 2149, Australia

SOURCE: Journal of Cell Science (1993), 105(3), 667-74

CODEN: JNCSAI; ISSN: 0021-9533

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Acidic and basic ~~fibroblast~~ growth factors (aFGF and bFGF) have been localized by immunochem. in ovine skin during wool follicle morphogenesis. At 40

days of gestation, prior to the appearance of follicle primordia, bFGF immunoreactivity was detected in the intermediate and periderm layers of the epidermis and at the dermal-epidermal junction. Antibodies to aFGF did not bind to skin at this age. During early follicle formation, at 76 days of gestation, both FGFs were found in the epidermis and associated with the follicle primordia. Antibodies to aFGF, in particular, bound to the basal cells of the epidermis and the follicle cell aggregations. With the development of epidermal plugs, bFGF was confined to the intermediate layers of the epidermis and the dermal-epidermal junction, whereas aFGF staining was associated with the cells of the epidermis and the plugs. At 90 days, when many different stages of follicle development were in evidence, immunoreactivity for both FGFs was associated with the cells of the elongating epidermal column, particularly those adjacent to the dermal-epidermal junction. During follicle maturation, bFGF was found in the suprabasal layer of the epidermis, in the outer root sheath of the follicle and in the basement membrane zone surrounding the bulb matrix. Conversely, strong staining for aFGF was observed in the epidermis and pilary canal contiguous with the epidermis, and in cells of the upper bulb matrix of the follicle in the region of the keratogenous zone. Western blotting of exts. of mature follicles that had been isolated from the skin showed the presence of a major aFGF immunoreactive band with an apparent mol. mass of 27 kDa. The distributions of aFGF and bFGF, particularly around the dermal-epidermal junction during follicle development, demonstrate that these growth factors may have related functions in local tissue remodelling during follicle morphogenesis. However, in adult skin, the presence of bFGF adjacent to the proliferative zone of the follicle suggests its involvement in regulating the mitotic activity in the follicle bulb. By contrast, the localization of aFGF to the cells of the upper follicle bulb, in the zone of keratinization, implicates this growth factor in cellular differentiation.

OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)

L21 ANSWER 37 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1994:213500 HCAPLUS Full-text

DOCUMENT NUMBER: 120:213500

ORIGINAL REFERENCE NO.: 120:37768h,37769a

TITLE: Localization of fibronectin in the rat testis: effects of serum and dibutyryl cyclic AMP on fibronectin deposition by peritubular myoid cells in culture

AUTHOR(S): Raychoudhury, Samir S.; Thompson, E.W.

CORPORATE SOURCE: Div. Sci. Technol., Griffith Univ., Brisbane, Australia

SOURCE: Molecular Andrology (1993), 5(4), 289-300  
CODEN: MOANE3

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of serum or dibutyryl cAMP on fibronectin (FN) production by the mesenchymal peritubular myoid cells were evaluated. Rats of various ages (10, 15, 20, 40, and 80 days) were employed for immunofluorescent localization of rat testicular FN in frozen sections. In all age groups tested, FN was primarily present in a broad layer around each seminiferous tubule, and blood vessel, and in variable distribution throughout the interstitial stroma. By day 20 there was no clear distinction in FN staining between the peritubular zone and the interstitial tissue. This indicates an involvement of FN in the extracellular matrix (ECM) development which occurs in the peritubular zone of the testis at this time. The peritubular myoid cells were isolated from 20-22-day-old rat testis and cultured on glass coverslips. These cells were grown to confluence with 10% fetal calf serum (FCS) in medium until day 4 and then subcultured to have secondary monocultures maintained with or without serum. By immunofluorescence and cytochem. using avidin-biotin peroxidase complex it was observed that peritubular myoid cells were pos. for FN and most of the FN was localized in the perinuclear region. Subcultured peritubular

myoid cells maintained for 4 days in medium containing FCS developed an extensive interconnecting FN ~~matrix~~. In the presence of 0.5 mM cAMP in culture, FN became localized along the filamentous process of peritubular myoid cells and more prominently in the areas of triangulated ~~multi-cell aggregates~~ as well as on the surface of the contracted small ~~spherical~~ cells. The addition of cAMP in the presence of FCS, also caused a noticeable change in the staining pattern; FN was detected along the filamentous process developing into a complex network of cells encased in an extensive ~~matrix~~. It would appear that the translocation of FN in the cytoplasmic extensions of peritubular myoid cells may be a direct consequence of morphol. changes associated with metabolic regulation of cAMP. This may also be related to the puberty-associated development of in vivo changes in the ECM produced by peritubular myoid cells.

L21 ANSWER 38 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1993:617847 HCAPLUS Full-text

DOCUMENT NUMBER: 119:217847

ORIGINAL REFERENCE NO.: 119:38593a,38596a

TITLE: Contact inhibition of cell spreading: a mechanism for the maintenance of thyroid cell aggregation in vitro

AUTHOR(S): Yap, Alpha S.; Manley, Simon W.

CORPORATE SOURCE: Dep. Physiol. Pharmacol., Univ. Queensland, St. Lucia, 4072, Australia

SOURCE: Experimental Cell Research (1993), 208(1), 121-7

CODEN: ECREAL; ISSN: 0014-4827

DOCUMENT TYPE: Journal

LANGUAGE: English

AB When freshly isolated porcine thyroid cells are stimulated with TSH they organize to form functional follicles in conventional substrate-adherent culture. Cell aggregation is essential for follicular reorganization and is likely to be influenced by the balance between cell-cell adhesion (promoting aggregation) and cell-substrate adhesion (favoring spreading and monolayer formation). Recently the authors observed that TSH potentiated cell-cell adhesion, and in the present study the authors have sought evidence that TSH might also regulate cell-substrate adhesion. Two parameters of cell-substrate adhesion, namely, cell attachment to collagen and cell spreading upon collagen, were measured using preps. of isolated single cells and of multicellular aggregates. TSH had no effect upon the attachment or spreading of single cells, but inhibited aggregate spreading without affecting aggregate attachment. The possibility that cell-cell contact modulated the response to TSH in aggregates, but not in single cells, was confirmed using a cell-free membrane preparation which inhibited the spreading of single cells but not their rate of attachment. Moreover, TSH potentiated the inhibitory effect of membranes on the spreading of single cells. Heparin also specifically inhibited the spreading of both single cells and cell aggregates,

suggesting that a heparin-sensitive adhesive mechanism might be recruited as thyroid cells spread. The authors conclude that thyroid cell-substrate adhesion is regulated by a synergistic interaction between cell-cell contact and TSH which preferentially inhibited cell spreading but not attachment. Such contact-dependent inhibition of cell spreading is predicted to preserve cell aggregates and hence contribute to the maintenance of thyroid follicular differentiation in vitro.

OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)

L21 ANSWER 39 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1991:4084 HCAPLUS Full-text

DOCUMENT NUMBER: 114:4084

ORIGINAL REFERENCE NO.: 114:826h,827a  
 TITLE: Maintenance on extracellular ~~matrix~~ and  
 expression of heparanase activity by human ovarian  
 carcinoma cells from biopsy specimens  
 AUTHOR(S): Peretz, Tamar; Antebi, Shaul U.; Beller, Uziel;  
 Horowitz, Aviva T.; Fuks, Zvi; Vlodavsky, Israel  
 CORPORATE SOURCE: Dep. Oncol., Hadassah Univ. Hosp., Jerusalem, Israel  
 SOURCE: International Journal of Cancer (1990),  
 45(6), 1054-60  
 CODEN: IJCNAW; ISSN: 0020-7136  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB A routine procedure has been developed for the isolation and maintenance in culture of human ovarian carcinoma cells derived from biopsy specimens. Cell attachment, plating efficiency and initial outgrowth were greatly improved by seeding the cells on a basement-membrane-like extracellular ~~matrix~~ (ECM) deposited by cultured corneal endothelial cells. These effects were most significant in serum-free conditions which markedly reduced the rate of cell attachment and growth on regular tissue culture plastic. In 60-80% of the cases, regardless of the patient's age, cells cultured on ECM in the absence of serum divided actively and formed a tightly packed epithelial cell ~~monolayer~~. Fibroblast over-growth and cell detachment often occurred on ECM in the presence of serum. Incubation of the human ovarian carcinoma cells with sulfate-labeled ECM, resulted in the release of heparan sulfate degradation fragments, 4- to 7-fold smaller than intact heparan sulfate side chains. This degradation was brought about by endoglycosidase (heparanase) activity expressed to a high extent by cells that were first maintained in primary cultures as compared with ~~cell aggregates~~ taken directly from the biopsy specimen. In most cases, cells derived from metastatic tumors expressed a higher heparanase activity than cells from the primary ovarian tumor. This result corroborates previous studies, performed with cell lines, on the possible involvement of heparanase in tumor cell invasion and metastasis. OS.CITING REF  
 COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD

(4 CITINGS)

L21 ANSWER 40 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN  
 ACCESSION NUMBER: 1988:505411 HCAPLUS Full-text  
 DOCUMENT NUMBER: 109:105411  
 ORIGINAL REFERENCE NO.: 109:17449a,17452a  
 TITLE: PC12 ~~cell aggregation~~ and dopamine  
 production on EHS-derived extracellular ~~matrix~~  
 AUTHOR(S): Bethea, Cynthia L.; Borg, Thomas K.  
 CORPORATE SOURCE: Div. Reprod. Biol. Behav., Oregon Reg. Primate Res.  
 Cent., Beaverton, OR, 97006, USA  
 SOURCE: Molecular and Cellular Endocrinology (1988),  
 58(2-3), 113-28  
 CODEN: MCEND6; ISSN: 0303-7207  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB PC12 cells on plastic grow as a ~~single-layered~~ lawn of ~~cells~~ which synthesize, store, and secrete dopamine. In contrast, PC12 cells cultured on Engelbreth-Holm-swarm (EHS) tumor-derived extracellular ~~matrix~~ grow into multicellular aggregates. ~~Matrix~~ dissoln. and cell migration appear to follow aggregate formation. PC12 cell plating efficiency is decreased on EHS- ~~matrix~~ but the doubling time of cells on EHS-~~matrix~~ is comparable to plastic. Dopamine secretion and cellular content determined with a radioenzymic assay as well as dopamine synthesis determined with cation-exchange chromatog. are similar on a per cell basis in cultures of PC12 cells on plastic and EHS-~~matrix~~. OS.CITING REF  
 COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD

(2 CITINGS)

L21 ANSWER 41 OF 41 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1987:117087 HCAPLUS Full-text

DOCUMENT NUMBER: 106:117087

ORIGINAL REFERENCE NO.: 106:19109a,19112a

TITLE: Morphogenetic restructuring and formation of basement membranes by Sertoli cells and testis peritubular cells in co-culture: inhibition of the morphogenetic cascade by cyclic AMP derivatives and by blocking direct cell contact

AUTHOR(S): Tung, Pierre S.; Fritz, Irving B.

CORPORATE SOURCE: Banting and Best Dep. Med. Res., Univ. Toronto, Toronto, ON, M5G 1L6, Can.

SOURCE: Developmental Biology (Orlando, FL, United States) (1987), 120(1), 139-53

CODEN: DEBIAO; ISSN: 0012-1606

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Addition of dibutyryl AMP (dbcAMP), methylisobutylxanthine (MIX), or cytochalasin D to co-cultures of Sertoli cells and testicular peritubular myoid cells blocks a series of morphogenetic changes which otherwise occur during culture. When Sertoli cells are plated directly onto preexisting layers of peritubular cells maintained under basal conditions, structures form which display many of the characteristics of germ cell-depleted seminiferous tubules. The presence of dbcAMP, MIX, or cytochalasin D, added at varying times after plating Sertoli cells, results in the inhibition of each successive stage of in vitro remodeling: the inhibition of migration of Sertoli cells, the inhibition of initial ridge formation, the blockage of subsequent formation of mounds and nodules of compacted Sertoli cell aggregates, the prevention of the formation of basal lamina and associated layers of extracellular matrix between Sertoli cell aggregates and surrounding peritubular cells, and the inhibition of tubule formation. The presence of dbcAMP also inhibits the migration of peritubular cells, contractions by these cells, and compaction of Sertoli cell aggregates. When intimate cell apposition is prevented by plating the 2 cell types on either side of a membrane filter, the morphogenetic cascade is blocked, and no formation of a germ cell-depleted seminiferous tubule-like structure occurs. Other effects of dbcAMP on cell shape, cell movement, and cell association patterns during co-culture are described. Possible mechanisms by which dbcAMP, MIX, or cytochalasin D blocks restructuring are discussed. Since each elicits perturbations of the cytoskeleton, the interpretation is offered that cytoskeletal changes may be correlated with the prevention of closely apposing cell compact and the inhibition of basement membrane formation. Interactions observed between Sertoli cells and peritubular cells during co-culture are postulated to be analogous to those occurring in other types of mesenchymal cell-epithelial cell interactions during organogenesis and during tubulogenesis in the fetal testis. Speculatively, the blockage by dbcAMP of the morphogenetic cascade in the co-cultured system may be related to the inhibition by dbcAMP of testis cord formation in organ cultures of fetal gonads reported by others. OS.CITING REF COUNT: 31 THERE ARE 31 CAPLUS RECORDS THAT CITE THIS

RECORD (31 CITINGS)

## SEARCH HISTORY

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(FILE 'HOME' ENTERED AT 11:14:52 ON 14 DEC 2010)

FILE 'HCAPLUS' ENTERED AT 11:15:15 ON 14 DEC 2010

E FORGACS GABOR/AU

L1 96 SEA ABB=ON ("FORGACS G"/AU OR "FORGACS GABOR"/AU)

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L2 13 SEA ABB=ON ("JAKAB K"/AU OR "JAKAB KAROLY"/AU OR "JAKAB KAROLY R"/AU OR "JAKAB KAROLY ROBERT"/AU)

E NEAGU ADRIAN/AU

L3 17 SEA ABB=ON "NEAGU ADRIAN"/AU

E MIRONOV VLADIMIR/AU

L4 130 SEA ABB=ON ("MIRONOV VLADIMIR"/AU OR "MIRONOV VLADIMIR A"/AU OR "MIRONOV VLADIMIR ALEKSEEVICH"/AU OR "MIRONOV VLADIMIR E"/AU OR "MIRONOV VLADIMIR F"/AU OR "MIRONOV VLADIMIR I"/AU OR "MIRONOV VLADIMIR N"/AU OR "MIRONOV VLADIMIR S"/AU OR "MIRONOV VLADIMIR SERGEYEVICH"/AU)

L5 3 SEA ABB=ON L1 AND L2 AND L3 AND L4

FILE 'HCAPLUS' ENTERED AT 11:16:41 ON 14 DEC 2010

L6 ANALYZE L5 1-3 CT : 21 TERMS

L7 745393 SEA ABB=ON ?BIOCOMPATIBL? OR ?MATRIX? OR ?MATRICES?

L8 588 SEA ABB=ON L7 AND CELL(W)AGGREGAT?

L9 172 SEA ABB=ON L8 AND (?SCAFFOLD? OR ?LAYER? OR ?THREE?(W)?DIMENSIONAL?)

L10 588 SEA ABB=ON L8 OR L9

L11 87 SEA ABB=ON L9 AND (NON(W)?RANDOM? OR ?CYLIND? OR ?SPHER? OR (?SINGL? OR ?MULT?)(3A)CELL? OR FIBROBLAST? OR ?MESENCHYMA?)

L12 588 SEA ABB=ON L10 OR L11

L13 104 SEA ABB=ON L12 AND (GEL? OR ?PHOTOSENSITIV? OR ?THERMO?(W)?REVERSIBL? OR PH(W)?SENSITIV?)

L14 87 SEA ABB=ON L11 AND (NON(W)?RANDOM? OR ?CYLIND? OR ?SPHER? OR (?SINGL? OR ?MULT?)(3A)CELL? OR FIBROBLAST? OR ?MESENCHYMA?)

L15 35 SEA ABB=ON L14 AND (PRD<20040224 OR PD<20040224)

FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 11:21:38 ON 14 DEC 2010

L16 168 SEA ABB=ON L15

FILE 'HCAPLUS' ENTERED AT 11:22:37 ON 14 DEC 2010

L17 19 SEA ABB=ON L11 AND (GEL? OR ?PHOTOSENSITIV? OR ?THERMO?(W)?REVERSIBL? OR PH(W)?SENSITIV?)

L18 87 SEA ABB=ON L14 OR L17

L19 35 SEA ABB=ON L18 AND (PRD<20040224 OR PD<20040224)

FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 11:24:56 ON 14 DEC 2010

L20 9 SEA ABB=ON L16 AND ?TISSUE?(W) ?ENGINEER?

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L21 41 DUP REMOV L19 L20 (3 DUPLICATES REMOVED)

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